Correction to: Rare variants in KDR, encoding VEGF Receptor 2, are associated with tetralogy of Fallot

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Abstract: Purpose: Rare genetic variants in KDR, encoding the vascular endothelial growth factor receptor 2 (VEGFR2), have been reported in patients with tetralogy of Fallot (TOF). However, their role in disease causality and pathogenesis remains unclear. Methods: We conducted exome sequencing in a familial case of TOF and large-scale genetic studies, including burden testing, in >1,500 patients with TOF. We studied gene-targeted mice and conducted cell-based assays to explore the role of KDR genetic variation in the etiology of TOF. Results: Exome sequencing in a family with two siblings affected by TOF revealed biallelic missense variants in KDR. Studies in knock-in mice and in HEK 293T cells identified embryonic lethality for one variant when occurring in the homozygous state, and a significantly reduced VEGFR2 phosphorylation for both variants. Rare variant burden analysis conducted in a set of 1,569 patients of European descent with TOF identified a 46-fold enrichment of protein-truncating variants (PTVs) in TOF cases compared to controls (P = 7 × 10-11). Conclusion: Rare KDR variants, in particular PTVs, strongly associate with TOF, likely in the setting of different inheritance patterns. Supported by genetic and in vivo and in vitro functional analysis, we propose loss-of-function of VEGFR2 as one of the mechanisms involved in the pathogenesis of TOF.

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CORRECTION

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Due to a processing error the author's Doris Škorić-Milosavljević, Najim Lahrouchi, Alex V. Postma, Connie R. Bezzina were assigned to affiliation 38. However, affiliation 38 does not exist.

In addition, the affiliations of Najim Lahrouchi, Elisabeth M. Lodder, and Connie R. Bezzina should be number 1 instead of number 2. The correct affiliation is Department of Clinical and Experimental Cardiology, Amsterdam University Medical Center, Amsterdam, The Netherlands.

The original article has been corrected.

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